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PALB2 Mutations

Cancer Risks and General Management Recommendations

Cancer Type	_PALB2_ Mutation Carrier Cancer Risks	General Population Lifetime Cancer Risks	Surveillance/Management Recommendations[1,2]

Female Breast[2-8]	Primary: 33-58% (risk dependent on family history)
	
	Second primary: Increased
		12.4%	*Surveillance*
			• Age 30 years: Annual mammogram with consideration of tomosynthesis and breast MRI with contrast
			  ○ Age to initiate breast surveillance may be modified based on family history (typically 5-10 years earlier than the youngest breast cancer diagnosis in the family, but no later than age 30)
			Surgery
			• Discuss option of risk-reducing mastectomy, including degree of protection, reconstruction options, and procedure-related risks
			  ○ Family history and residual breast cancer risk with age and life expectancy should be considered

Pancreas	Increased[3,9] (lifetime risk unknown)	<1%	*Surveillance*
			• Age 50 years: Consider surveillance using annual abdominal MRI/MRCP, EUS, and/or enrollment in research protocols for individuals with pancreatic cancer in ≥1 first- or second-degree relative from the same side of the family as the *PALB2* mutation
			  ○ Age to initiate pancreatic surveillance may be modified based on family history (10 years younger than the earliest diagnosis in the family)
			  ○ In absence of a close family history of pancreatic cancer, no pancreatic screening is currently recommended

Other Cancer Risks: While the potential for additional cancer risks has been suggested, at this time, no additional cancer risks have been well established. A potential increased risk of ovarian cancer has been suggested, but there is insufficient evidence for risk-reducing salpingo-oophorectomy and management should be based on family history. [1] Cancer risks and management recommendations may evolve over time.

PARP Inhibitors: Recent studies have identified PARP inhibitors as a potential chemotherapeutic agent for *BRCA*-associated breast, ovarian, pancreatic and metastatic prostate cancers. Clinical trials are currently in process to determine how this agent can best be used clinically, and these agents may prove to be effective in *PALB2* related cancers in the future.[9] Patients should speak with their treating physicians for more information regarding PARP inhibitors.

Implications for Family Members/Reproductive Considerations

- First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the familial *PALB2* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation.
- Rarely, individuals inherit two *PALB2* mutations (one from each parent), and have Fanconi Anemia (FA). [10]
  - FA is characterized by physical abnormalities as well as pediatric leukemia and other cancers.
  - *PALB2* genetic testing for the partner of an individual with a *PALB2* mutation may be appropriate to clarify the risk of having a child with FA.
- For carriers of a known mutation, assisted reproduction (with or without egg or sperm donation), pre-implantation genetic testing, and prenatal diagnosis options exist.
- All family members are encouraged to pursue genetic counseling to clarify their risks. Family members can visit www.FindAGeneticCounselor.com to find genetic services near them.

References

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